as a CPA of application 08/031,801, filed March 15, 1993. It, therefore, qualifies for the transitional procedures for examination after final rejection set forth in 37 C.F.R. § 1.129(a).

Rule 129(a) states that applicant is entitled to have a submission entered and considered on the merits after final rejection, if the submission and the fee set forth in 37 C.F.R. § 1.17(r) are filed prior to the filing of an appeal brief or abandonment of the application. The Rule further states that the finality of the rejection is automatically withdrawn upon the timely filing of the submission and the payment of the fee set forth in § 1.17(r).

Applicants submit the required fee and request that the finality of the outstanding Action be removed and that the Examiner enter and consider this amendment and response.

Kindly amend the application as follows.

IN THE CLAIMS

Add claims 104-109, cancel claims 89-~~94~~, 101-~~103~~, without prejudice, and amend the remaining claims as shown below:

83. A transgenic [nonprimate mammal] mouse comprising in its germline a modified genome wherein said modification comprises [a lesion in the J region of at least one copy of the immunoglobulin heavy chain locus, wherein said lesion results in the inability of said copy of the locus to rearrange or to produce a functional message encoding an immunoglobulin heavy-chain subunit] inactivated endogenous immunoglobulin heavy chain loci in which all of the J segment genes from both copies of the immunoglobulin heavy chain locus are deleted to prevent

rearrangement and to prevent formation of a transcript of a rearranged locus and the expression of an endogenous immunoglobulin heavy chain from the inactivated loci.

84. The [mammal] mouse of claim 83 wherein said modification further comprises [a lesion in the an J or constant region or both of at least one copy of an immunoglobulin light-chain locus, said lesion resulting in the inability of said locus to rearrange or to produce a functional message encoding said light-chain subunit] an inactivated endogenous immunoglobulin light chain locus in which all of the J segment genes from at least one copy an immunoglobulin light chain locus are deleted to prevent rearrangement and to prevent formation of a transcript of a rearranged locus and the expression of an endogenous immunoglobulin light chain from the inactivated locus.

85. The [mammal] mouse of claim 83 wherein said modification comprises [said lesions in two copies of the immunoglobulin heavy-chain locus or further comprises said lesions in two copies of said immunoglobulin light-chain locus or both] inactivated endogenous immunoglobulin light chain loci in which all of the J segment genes from both copies of the immunoglobulin light chain locus are deleted to prevent rearrangement and to prevent formation of a transcript of a rearranged locus and the expression of an endogenous immunoglobulin light chain from the inactivated loci.

86. The [mammal] mouse of claim 83 wherein said modification further comprises inclusion of, in said genome, an immunoglobulin locus encoding a xenogeneic light chain or

xenogeneic heavy chain or both;

wherein said xenogeneic heavy chain comprises a DNA sequence identical to the germline DNA sequence of human chromosome 14 from the D segment genes of the human immunoglobulin heavy chain locus, continuing through the J segment genes and the constant region genes through Cμ of that locus, wherein said DNA sequence does not include a gamma constant region, and wherein said DNA fragment is operably linked to at least one human V segment gene.

87. The [mammal] mouse of claim 84 wherein said modification further comprises inclusion of, in said genome, an immunoglobulin locus encoding a xenogeneic light chain or xenogeneic heavy chain or both;

wherein said xenogeneic heavy chain comprises a DNA sequence identical to the germline DNA sequence of human chromosome 14 from the D segment genes of the human immunoglobulin heavy chain locus, continuing through the J segment genes and the constant region genes through Cμ of that locus, wherein said DNA sequence does not include a gamma constant region, and wherein said DNA fragment is operably linked to at least one human V segment gene.

88. The [mammal] mouse of claim 85 wherein said modification further comprises inclusion of, in said genome, an immunoglobulin locus encoding a xenogeneic light chain or xenogeneic heavy chain or both;

wherein said xenogeneic heavy chain comprises a DNA sequence identical to the germline DNA sequence of human chromosome 14 from the D segment genes of the human

immunoglobulin heavy chain locus, continuing through the J segment genes and the constant region genes through Cμ of that locus, wherein said DNA sequence does not include a gamma constant region, and wherein said DNA fragment is operably linked to at least one human V segment gene.

95. The transgenic [nonprimate mammal] mouse of claim 86 wherein the xenogeneic light chain immunoglobulin locus is human.

96. The transgenic [nonprimate mammal] mouse of claim 87 wherein the xenogeneic light chain immunoglobulin locus is human.

97. The transgenic [nonprimate mammal] mouse of claim 88 wherein the xenogeneic light chain immunoglobulin locus is human.

104. The mouse of claim 83 wherein said modification further comprises inclusion of, in said genome, an immunoglobulin locus encoding a xenogeneic light chain or xenogeneic heavy chain or both;

wherein said xenogeneic heavy chain comprises a DNA sequence that is derived from and contains a germline DNA sequence of human chromosome 14 from the D segment genes of the human immunoglobulin heavy chain locus, continuing through the J segment genes and the constant region genes through Cμ of that locus, wherein said DNA sequence does not include a gamma constant region, and wherein said DNA fragment is operably linked to at least one human V segment gene.

105. The mouse of claim 84 wherein said modification further comprises inclusion of, in said genome, an immunoglobulin locus encoding a xenogeneic light chain or xenogeneic heavy chain or both;

wherein said xenogeneic heavy chain comprises a DNA sequence that is derived from and contains a germline DNA sequence of human chromosome 14 from the D segment genes of the human immunoglobulin heavy chain locus, continuing through the J segment genes and the constant region genes through Cμ of that locus, wherein said DNA sequence does not include a gamma constant region, and wherein said DNA fragment is operably linked to at least one human V segment gene.

106. The mouse of claim 85 wherein said modification further comprises inclusion of, in said genome, an immunoglobulin locus encoding a xenogeneic light chain or xenogeneic heavy chain or both;

wherein said xenogeneic heavy chain comprises a DNA sequence that is derived from and contains a germline DNA sequence of human chromosome 14 from the D segment genes of the human immunoglobulin heavy chain locus, continuing through the J segment genes and the constant region genes through Cμ of that locus, wherein said DNA sequence does not include a gamma constant region, and wherein said DNA fragment is operably linked to at least one human V segment gene.

107. The transgenic mouse of claim 86 wherein the xenogeneic light chain immunoglobulin locus is human.

108. The transgenic mouse of claim 87 wherein the